



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Longgui WANG et al.

Confirmation No.:

Application No.: 10/673,426

Group Art Unit:

Filing Date: September 30, 2003

Examiner:

For: METHOD OF MODULATING IMMUNE  
RESPONSE BY ADMINISTRATION OF  
IMMUNO-ACTIVATION AGENT

Attorney Docket No.: 81481-200

**SUBSTITUTE INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

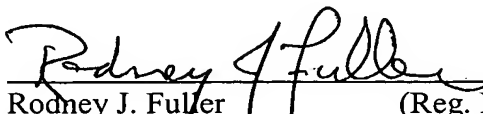
Pursuant to Applicants' duty of disclosure under 37 C.F.R. §1.56, Applicants submit the enclosed Form PTO-1449 listing twenty-nine (29) references for the Examiner's review and consideration. Copies of references B1 through B26 are also enclosed for the Examiner's convenience. Copies of U.S. patent references A1 through A3 will be provided if the Examiner so requests.

It is respectfully requested that the references be made of record in this application by the Examiner's completion and return of Form PTO-1449. It is further requested that this Information Disclosure Statement ("IDS") be treated in its entirety as a substitute for the IDS originally filed on September 30, 2003 as an enclosure to the subject application.

No fee is believed to be due for the submission of this IDS. Should any fees be required, however, please charge such fees to Winston & Strawn LLP's Deposit Account No. 50-1814.

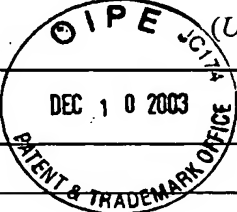
Respectfully submitted,

12/10/03  
Date

  
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For: Allan A. Fanucci (Reg. No. 30,256)

**WINSTON & STRAWN LLP**  
Customer No. 28765

202-371-5838

<b>LIST OF REFERENCES CITED BY APPLICANT</b> <b>Form PTO-1449</b> <i>(Use several sheets if necessary)</i>		ATTY. DOCKET NO.:	APPLICATION NO.:
		81481-200	10/673,426
		APPLICANT:	
		Jen-Wei CHIAO et al.	
Sheet 1 of 2		FILING DATE:	GROUP:
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U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL	CITE NO.	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A1	5,231,209	7/1993	Chung et al.	558	17	
	A2	6,348,220	2/2002	Ribnicky et al.	424	725	
	A3	6,433,011	8/2002	Chung et al.	514	514	

		OTHER REFERENCES <i>(Including Author, Title, Date, Pertinent Pages, Etc.)</i>
	B1	Brusewitz, G., Cameron, B.D., Chasseaud, L.F., Gorler, K., Hawkins, D.R., Koch, H., and Mennicke, W.H. (1977) The metabolism of benzyl isothiocyanate and its cysteine conjugate. The Biochemical Journal, 162: 99-107.
	B2	Chen, Y.R., Han, J., Kori, R., Kong, A.N., and Tan, T.H. (2002) Phenylethyl isothiocyanate induces apoptotic signaling via suppressing phosphatase activity against c-Jun N-terminal kinase. J Biol Chem, Oct.18; 277(42): 39334-39342.
	B3	Chiao, J.W., Chung, F., Krzeminski, J., Amin, S., Arshad, R., Ahmed, T., and Conaway, C.C. (2000) Modulation of growth of human prostate cancer cells by the N-acetylcysteine conjugate of phenethyl isothiocyanate. International Journal of Oncology, 16: 1215-1219.
	B4	Chiao, J.W., Chung, F.L., Kancherla, R., Ahmed, T., Mittelman, A., and Conaway, C.C. (2002) Sulforaphane and its metabolite mediate growth arrest and apoptosis in human prostate cancer cells. International Journal of Oncology, 20: 631-636.
	B5	Chung, F.-L. (1992) "Chemoprevention of lung carcinogenesis by aromatic isothiocyanates." In: Cancer Chemoprevention, Edition, (eds., Wattenberg, L., Lipkin, M., Boone, C.W., Kelloff, G.J.) pp. 227-245, CRC Press Inc.
	B6	Chung, F.L., Conaway, C.C., Rao, C.V., and Reddy, B.S. (2000) Chemoprevention of colonic aberrant crypt foci in Fischer rats by sulforaphane and phenethyl isothiocyanate. Carcinogenesis, 21(12): 2287-2291.
	B7	Chung, F.-L., Morse, M.A., and Eklind, K.I. (1992) New potential chemopreventive agents for lung carcinogenesis of tobacco-specific nitrosamine. Cancer Research, 52: 2719s-2722s, 1992.
	B8	Chung, F.L., Morse, M.A., Eklind, K.I., and Lewis, J. (1992) Quantitation of human uptake of the anticarcinogen phenethyl isothiocyanate after a watercress meal. Cancer Epidemiology, Biomarkers & Prevention: A Publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, 1: 383-388.
	B9	Conaway, C.C., Jiao, D., and Chung F.L. (1996) Inhibition of rat liver cytochrome P450 isozymes by isothiocyanates and their conjugates: a structure-activity relationship study. Carcinogenesis, 17(11): 2423-2427.
	B10	Eklind, K.I., Morse, M.A., and Chung, F.L. (1990) Distribution and metabolism of the natural anticarcinogen phenethyl isothiocyanate in A/J mice. Carcinogenesis, 11: 2033-2036.
	B11	Hecht, S.S. (1995) Chemoprevention by isothiocyanates. Journal of Cellular Biochemistry (Suppl.), 22: 195-209.
	B12	Hecht, S.S., Upadhyaya P., Wang, M., Bliss, R.L., McIntee, E.J., and Kenney, P.M. (2002) Inhibition of lung tumorigenesis in A/J mice by N-acetyl-S-(N-2-phenethylthiocarbamoyl)-L-cysteine and myo-inositol, individually and in combination. Carcinogenesis, 23(9): 1455-1461.

EXAMINER	DATE CONSIDERED
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

DC-331416.1

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OTHER REFERENCES <i>(Including Author, Title, Date, Pertinent Pages, Etc.)</i>	
B13	Hunter, T. and Pines, J. (1994) Cyclins and cancer. II: Cyclin D and CDK inhibitors come of age. <i>Cell</i> , 79: 573-582.
B14	Jiao, D., Conaway, C.C., Wang, M.H., Yang, C.S., Koehl, W., and Chung, F.L. (1996) Inhibition of N-nitrosodimethylamine demethylase in rat and human liver microsomes by isothiocyanates and their glutathione, L-cysteine, and N-acetyl-L-cysteine conjugates. <i>Chemical Research in Toxicology</i> , 9: 932-938.
B15	Kassahun, K., Davis, M., Hu, P., Martin, B., and Baillie, T. (1997) Biotransformation of the naturally occurring isothiocyanate sulforaphane in the rat: identification of phase 1 metabolites and glutathione conjugates. <i>Chemical Research in Toxicology</i> , 10: 1228-1233.
B16	Mattes, M.J., Sharrow, S.O., Herberman, R.B., and Holden, H.T. (1979) Identification and separation of Thy-1 positive mouse spleen cells active in natural cytotoxicity and antibody-dependent cell-mediated cytotoxicity. <i>Journal of Immunology</i> , 123: 2851-2860.
B17	Morgan, D.O. (1995) Principles of CDK regulation. <i>Nature</i> , 374: 131-134.
B18	Sherr, C.J. (2000) The Pezcoller lecture: cancer cell cycles revisited. <i>Cancer Research</i> , 60: 3689-3695.
B19	Sherr, C.J. and Roberts, J.M. (1999) CDK inhibitors: positive and negative regulators of G1-phase progression. <i>Genes and Development</i> , 13: 1501-1512.
B20	Stoner, G.D., Morrissey, D.T., Heur, Y.-H., Daniel, E.M., Galati, A.J., and Wagner, S.A. (1991) Inhibitory effects of phenethyl isothiocyanate on N-nitrosobenzyl-methylamine carcinogenesis in the rat esophagus. <i>Cancer Research</i> , 51: 2063-2068.
B21	Telford, W.G., King, L.E., and Fraker, P.J. (1992) Comparative evaluation of several DNA binding dyes in the detection of apoptosis-associated chromatin degradation by flow cytometry. <i>Cytometry: the Journal of the Society for Analytical Cytology</i> , 13: 137-143.
B22	Wang, L.G., Liu, X.M., Kreis, W., and Budman, D.R. (1999) Phosphorylation/ dephosphorylation of androgen receptor as a determinant of androgen agonistic or antagonistic activity. <i>Biochemical and Biophysical Research Communications</i> , 259: 21-28.
B23	Wattenberg, L.W. (1977) Inhibition of carcinogenic effects of polycyclic hydrocarbons by benzyl isothiocyanate and related compounds. <i>Journal of the National Cancer Institute</i> , 58: 396-398.
B24	Yang, C.S., Smith, T.J., and Hong, J.Y. (1994) Cytochrome P-450 enzymes as targets for chemoprevention against chemical carcinogenesis and toxicity: opportunities and limitations. <i>Cancer Research</i> , 54: 1982s-1986s.
B25	Yang, Y.M., Conaway, C.C., Chiao, J.W., Wang, C.X., Amin, S., Whysner, J., Dai, W., Reinhardt, J., and Chung, F.L. (2002) Inhibition of benzo(a)pyrene-induced lung tumorigenesis in A/J mice by dietary N-acetylcysteine conjugates of benzyl and phenethyl isothiocyanates during the postinitiation phase is associated with activation of mitogen-activated protein kinases and p53 activity and induction of apoptosis. <i>Cancer Research</i> , 62: 2-7.
B26	Zhang, Y. and Talalay, P. (1994) Anticarcinogenic activities of organic isothiocyanates: chemistry and mechanisms. <i>Cancer Research (Suppl.)</i> , 54: 1976s-1986s.

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